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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/473,789	06/07/95	CURTISS	REGAN-100-21

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EXAMINER, V

ART UNIT 1802 PAPER NUMBER

10

DATE MAILED: 04/15/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-38 is/are pending in the application.

Of the above, claim(s) 5-7, 15, 17-19, 21-22, 25, 26, 30-36, 38 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-4, 8-14, 16, 20, 23, 24, 27-29, 37 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892 (2 pages)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Part III DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group I (claims 1-29) and species C (claims 13 and 14) in Paper No. 9 is acknowledged. The traversal is on the ground(s) that Applicant has amended claim 30 to require both an essential gene and a lethal gene. In addition, Applicant asserts that all of the pending claims (claims 1-38) read on the elected invention. Applicants further asserts that the requirement for election of species appears to be improperly drawn; the species groups are not mutually exclusive from each other. In addition, Applicant submits that to be valid, a restriction requirement must establish both that (1) the "inventions" are either independent or distinct, and (2) that examination of more than one of the "inventions" would constitute a burden to the Examiner. Since claim 30 was amended to require both an essential gene and a lethal gene, the restriction of the two groups is withdrawn. However, the restriction of the species is still proper. Applicant's arguments pertaining to the species restriction is not found persuasive because Applicant has noted that the Office Action mailed October 18, 1996 sets forth reasons why the "species" are distinct. In addition, the MPEP 806.04(f) states:

"The general test as to when claims are restricted,

respectively, to different species is the fact that one claim recites limitations which under the disclosure are found in a first species but not in a second, while a second claim recites limitations disclosed only for the second species and not the first."

The restriction as set forth is to:

Species A, directed to a cell having a regulatory gene down regulating the lethal gene in a permissive environment.

Species B, directed to a cell having a regulatory gene up regulating the lethal gene in a non-permissive environment.

Species C, directed to a cell having a regulatory gene down regulating the essential gene in a non-permissive environment.

Species D, directed to a cell having regulatory gene up regulating the essential gene in a permissive environment.

Species E, directed to a cell having a regulatory gene down regulating the replicative gene in a non-permissive environment.

Species F, directed to cell having a regulatory gene up regulating the replicative gene in a permissive environment.

Since a search of the "species" would require a divergent literature and patent search, and a search for up regulation would not encompass a search for down regulation, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made **FINAL.**

In this application:

Claims 5 and 30 were amended.

Claims 36-38 were added.

Claims 5-7, 15, 17-19, 21-22, 25, 26, 30-36 are withdrawn from further consideration.

Claims 1-4, 8-14, 16, 20, 23, 24, 27-29, and 37 are now pending and under examination.

Claim Rejections - 35 USC § 112

Claims 1-4, 8-14, 16, 20, 23, 24, 27-29, and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of some Salmonella strains as a vaccine, does not reasonably provide enablement for the use of all attenuated strains of Salmonella as a vaccine.

Cardenas et al (Clinical Microbiology Reviews 5(3):328-342, 1992) teach that Salmonella strains with a mutation in the asd

gene are avirulent for mice by all routes of inoculation, but their survival time in the GALT is so limited that their immunogenicity is very reduced. (See especially page 333, first column)

In addition, Cardenas et al indicate that some mutations so attenuate the organisms as to make them unsuitable for use in live vaccines. (See especially page 332)

Sigwart et al (Infection and Immunity 57(6):1858-1861, 1989) also teach that purA mutations decrease the virulence of Salmonella strains, but it so attenuates the organisms as to make them unsuitable for use in live vaccines. (See especially page 1860)

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim Rejections

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-3, 10-13, 16, 20, 23, 24, 27, 28, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerdes et al.

The claims are directed to a microbial cell comprising an Environmentally Limited Viability System.

Gerdes et al (Proc Natl Acad Sci 83:3116-3120, 1986) disclose *Escherichia coli* bacteria with a sok gene and a hok gene. The hok gene encodes a highly toxic gene product whose overexpression causes a rapid killing of the host cell whereas the sok gene suppresses the hok gene. (See especially Abstract and page 3119)

In addition, Gerdes et al disclose that the sok gene is not activated at 30 C. However, the Sok+ phenotype is expressed at 42 C.

It is noted that claims 27, and 28 are to a method of making a cell strain. However, the claims contain no limitations that further differentiate the method of making the cell from the cell.

Thus, the prior art disclosure is viewed as anticipating the claimed invention.

Claims 1-4, 10-12, 23, 24, and 27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Curtiss.

The claims are directed to a microbial cell comprising an Environmentally Limited Viability System.

Curtiss (US Patent 4,190,495) disclose a *E. coli* with polA and recA. (See especially column 5)

Furthermore, Curtiss disclose that the combination of recA and pol A cause rapid degradation of DNA at 32C and below. Therefore, rapid destruction of genetic information occurs in microorganisms that escape to all environments other than within a warm-blooded animal.

The term "vaccine" is viewed as an intended use for the cell as the claims do not contain any further limitations that differentiate the composition from the prior art.

It is noted that claims 27, and 28 are to a method of making a cell strain. However, the claims contain no limitations that further differentiate the method of making the cell from the cell.

Thus, the prior art disclosure is viewed as anticipating the claimed invention.

Claims 1-3, 8, 10-14, 16, 20, 27, 28, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerdes et al.

Gerdes et al (EMBO Journal 5(8):2023- 2029, 1986) disclose an *E. coli* cell with a parB region that encodes the hok and sok gene. (See especially Abstract)

Furthermore, Gerdes et al disclose that the parB region and the relB operon were cloned into oriC minichromosomes.

It is noted that claims 27, and 28 are to a method of making a cell strain. However, the claims contain no limitations that further differentiate the method of making the cell from the cell.

Thus, the prior art disclosure is viewed as anticipating the claimed invention.

Claims 1, 4, 10-14, 20, 23, 24, 27, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Ramos et al.

Ramos et al (Bio/Technology 13:35-37, 1995) disclose a *Pseudomonas putida* strain that contained an *E. coli* lacI gene under the control of the Pm promoter, and the xylS gene. It also contained the Plac::gef fusion. (See especially page 36, second column)

Ramos et al also disclose another system that consisted of the hok gene under the control of the *E. coli* trp promoter. (See especially page 36, first column)

In addition, Ramos et al disclose that suicide genes such as hok and gef can be inserted next to the switch promoter fim Ap16 in *E. coli*, either on plasmids or integrated into the chromosome.

Furthermore, Ramos et al disclose that engineered strains of *Salmonella* sp and *E. coli* are being considered as live vaccines.

It is noted that claims 27, and 28 are to a method of making a cell strain. However, the claims contain no limitations that further differentiate the method of making the cell from the cell.

The term "vaccine" is viewed as an intended use for the cell as the claims do not contain any further limitations that differentiate the composition from the prior art.

Thus, the prior art disclosure is viewed as anticipating the claimed invention.

The Art Unit location of your application in the Patent and Trademark Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1802.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to V. Ryan whose telephone number is (703)305-6558.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted to the Group 1800 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette,

1096 OG 30 (November 15, 1989). The fax number for Art Unit 1802 is (703)308-4242.

V. Ryan
Patent Examiner/Art Unit 1802
March 3, 1997
Ryan/vr

James C. Housel
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GROUP 180